

Claims

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1. A method for preventing or treating a disease or condition caused, or contributed to, by TNF- $\alpha$ -induced lipolysis or elevated FFA levels in an subject, comprising administering to the subject a pharmaceutically effective amount of an inhibitor of a MAPK pathway to reduce lipolysis, to thereby prevent or treat the disease or condition in the subject.

2. The method of claim 1, wherein the inhibitor is sodium salicylate.

3. The method of claim 1, wherein the inhibitor is a direct inhibitor.

4. The method of claim 3, wherein the inhibitor decreases the protein level of ERK1/2 and/or a JNK.

5. The method of claim 4, wherein the inhibitor decreases expression of a gene encoding ERK1/2 and/or a JNK.

6. The method of claim 5, wherein the inhibitor interacts with an ERK1/2 and/or JNK gene.

7. The method of claim 4, wherein the inhibitor is an antisense molecule, a triplex molecule, or a ribozyme.

8. The method of claim 3, wherein the inhibitor decreases the activity of ERK1/2 and/or a JNK.

9. The method of claim 6, wherein the inhibitor interacts with ERK1/2 and/or a JNK protein.

10. The method of claim 6, wherein the inhibitor inhibits ERK1/2 and/or JNK phosphorylation.

11. The method of claim 1, wherein the inhibitor of the MAPK pathway does not interact with a PPAR- $\gamma$  receptor.

12. The method of claim 1, further comprising administering to the subject an inhibitor of the ERK/MAP kinase pathway.

13. A method for treating a subject having insulin resistance, comprising administering to the subject a pharmaceutically effective amount of an inhibitor of ERK1/2 and/or JNK pathway in an amount sufficient to decrease TNF- $\alpha$ -induced lipolysis.

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- ~~14.~~ A method for treating a subject having NIDDM, comprising administering to the subject a pharmaceutically effective amount of an inhibitor of the ERK1/2 and/or JNK pathway in an amount sufficient to decrease TNF- $\alpha$ -induced lipolysis.
- ~~15.~~ A method for determining whether a subject has or is likely to develop a disease or condition caused, or contributed to, by lipolysis, comprising determining the activity of an ERK1/2 and/or JNK in the individual, and wherein an abnormally high ERK1/2 and/or JNK activity indicates that the individual has or is likely to develop a disease or condition caused, or contributed to, by lipolysis.
16. The method of claim 15, wherein determining the activity of an ERK1/2 and/or JNK comprises determining the ERK1/2 and/or JNK protein level, and wherein an abnormally high ERK1/2 and/or JNK protein level is an abnormally high ERK1/2 and/or JNK activity.
17. The method of claim 15, wherein determining the activity of an ERK1/2 and/or JNK comprises determining whether the ERK1/2 and/or JNK protein is a mutated ERK1/2 and/or JNK protein.
- ~~18.~~ A drug screening method for identifying a compound which reduces TNF- $\alpha$  induced lipolysis comprising
- (i) isolating a compound which is an ERK1/2 and/or JNK inhibitor;
  - (ii) contacting an adipocyte with the compound of step (i) and TNF- $\alpha$  and determining the level of lipolysis, wherein a lower level of lipolysis in the presence of the compound of step (i) relative to the level of lipolysis in the absence of the compound of step (i) indicates that the compound reduces lipolysis,
- to thereby identify a compound which reduces lipolysis.

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